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Ambient Water Quality Criteria Pentachlorophenol

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PENTACHLOROPHENOL

Ambient Water Quality Criteria

Criteria and Standards Division
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CRITERION DOCUMENT

PENTACHLOROPHENOL

CRITERIA

Aquatic Life

For pentachlorophenol the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 6.2 µg/l as a 24-hour average and the concentration should not exceed 14 µg/l at any time.

For pentachlorophenol the criterion to protect saltwater aquatic life as derived using the Guidelines is 3.7 µg/l as a 24-hour average and the concentrations should not exceed 8.5 µg/l at any time.

Human Health

For the protection of human health from the toxic properties of pentachlorophenol ingested through water and through contaminated aquatic organisms, the ambient water quality criterion is determined to be 140 µg/l.

BIBLIOGRAPHIC INFORMATION

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Ambient Water Quality Criteria: Pentachlorophenol.

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for pentachlorophenol. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itsel , ...

KEYWORDS: *Water quality, *Toxicology, *Water pollution effects(Humans), *Water pollution effects(Animals), *Toxic substances, *PCP herbicide, *Phenol/pentachloro.

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Introduction

Pentachlorophenol (PCP) is a commercially produced bactericide, fungicide, and slimicide used primarily for the preservation of wood, wood products, and other materials. As a chlorinated hydrocarbon, its biological properties have also resulted in its use as an herbicide, insecticide, and molluscicide.

Pentachlorophenol (PCP) is a substituted phenol prepared by the chlorination of phenol in the presence of a catalyst. PCP has the empirical formula C_6Cl_5OH, a molecular weight of 266.35, a density of 1.978, and a vapor pressure of 0.12 mm Hg at 100 degrees C (Stecher, 1968; Natl. Fire Prot. Assoc., 1973; Sax, 1975; Spector, 1956). The melting point of pentachlorophenol ranges between 190 and 191 degrees C for the anhydrous form (Stecher, 1968; Weast, 1975-76). PCP decomposes at its boiling point of 309 to 310 degrees C (Stecher, 1968). PCP behaves as a weak acid and is readily disassociated to form the corresponding salt in an alkaline solution.

PCP is slightly soluble in water (14 mg/l at 20 degrees C) while its alkaline salts such as sodium pentachlorophenate (Na-PCP) are highly soluble in water (Weast, 1975-76).

It has been shown that commercial preparations of PCP contain certain "caustic insolubles" or "nonphenolic, neutral impurities," such as tetra-, penta-, hexa-, hepta-, and octachlorodibenzofurans and the octachlorodibenzo-p-dioxins (Johnson, et al. 1973). The chemically pure PCP used in comparative studies had no detectable concentrations of any chlorinated dioxins.

PCP is known to undergo photochemical degradation in solution in the presence of sunlight with the subsequent formation of several chlorinated benzoquinones, 2,4,5,6-tetrachlororesorcinol, and chloranilic acid (Mitchell, 1961; Hanadmad, 1967). Na-PCP is decomposed directly by sunlight with the formation of numerous products including oxidized monomers, dimers, a trimer, and chloranilic acid (Munakata and Kuwahara, 1969; Haitt, et al. 1960). Wong and Crosby (1977) reported the degradation by sunlight or ultraviolet light of dilute solutions of pentachlorophenol to lower chlorophenols, tetrachlorodihydroxyl benzenes, and non-aromatic fragments such as dichloromaleic acid. The irradiation of Na-PCP in relatively high concentrations in aqueous solutions has been reported to form octachlorodibenzo-p-dioxin (Wong and Crosby, 1977).

Although Ingols, et al. (1966) observed no alteration of Na-PCP by activated sludge microbes after 4 days of incubation, Watanabe (1973) reported the growth of an isolated species of Pseudomonas from PCP-perfused culture samples using PCP as the sole carbon source. Other microorganisms also have been isolated and reported to metabolize PCP (Suzuki and Nose, 1971; Cserjesi, 1967). The microbial degradation of Na-PCP to carbon dioxide and chloride ions was demonstrated using mixed microbial communities and an axenic bacterial culture (Reiner, et al. 1977).

Studies of PCP bioconcentration by aquatic life indicate factors ranging from 13 (Parrish, et al. 1978) to 1,000 (Kobayaski and Akitake, 1975) for freshwater and marine vertebrates.

Although PCP and Na-PCP are both highly toxic and widely disseminated in the environment, there is a paucity of data on their environmental concentration, fate, and effects. Their principal use as a wood preservative results in both point source water contamination at manufacturing and wood preservation sites and, conceivably, non-point source water contamination through runoff wherever there are PCP-treated lumber products exposing PCP or Na-PCP to soil. Raw and finished drinking waters have been found to have PCP levels of 0.17 and 0.06 µg/l, respectively (Butler, et al. 1973). Harvey and Crafts (1952) noted that PCP persisted in warm, moist soils for a period of 12 months.

PCP and its sodium salt, sodium pentachlorophenate (Na-PCP), have been demonstrated to be highly toxic to man, mammals, and aquatic life. As a result of their toxic nature, accumulation in tissues, and widespread industrial and agricultural applications, both PCP and Na-PCP pose a potential threat to terrestrial and aquatic life.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Pentachlorophenol (PCP), including its sodium salt, represents one of the most widely used pesticides in the United States. It is used as an algicide, bactericide, fungicide, herbicide, and insecticide.

Prior to 1960 the high toxicity of PCP to aquatic organisms was generally recognized, but few toxicity tests had been conducted with aquatic organisms. Almost all toxicity tests with PCP have been acute, and, except for one test with the saltwater sheepshead minnow, no chronic test data are available.

One likely reason for the lack of chronic toxicity tests is the relatively low environmental persistence of PCP as compared to DDT and similar chlorinated hydrocarbon insecticides. This also may account for the paucity of data on bioconcentration of PCP.

In spite of an apparently high degree of phytotoxicity there are few studies on the toxicity of PCP to aquatic plants.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] and the Methodology Document in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

Acute Toxicity

Nearly 60 determinations of 96-hour LC50 values for fish and PCP are listed in Table 1; however, more than half are from a single study dealing with two species (Adelman and Smith, 1976). Of the remaining LC50 values only five are from flow-through tests with measured concentrations.

There are few specific data upon which to determine the relationship between LC50 values based on unmeasured and measured levels or between LC50 values based on static and flow-through tests. Toxicity tests with sockeye salmon yielded 96-hour LC50 values of 50 and 130 µg/l in static tests (Davis and Hoos, 1975) and of 63 µg/l in a flow-through test (Webb and Brett, 1973). Since all values were based on unmeasured concentrations of PCP, no conclusions are possible.

Toxicity tests with bluegill yielded 96-hour LC50 values of 60 and 77 µg/l in unmeasured static tests (Pruitt, et al. 1977). These data are enigmatic, since there is no likely rationale to explain the higher LC50 values based on measured values than those LC50 values based on unmeasured values. The two likely explanations, significant differences in test conditions between the two studies or experimental variability, render the comparison of these data difficult.

A final potential comparison of test methods is available with the data for fathead minnows. Mattson, et al. (1976) found a 96-hour LC50 of 600 µg/l in a single static, unmeasured test, and several other investigators reported 96-hour LC50 values ranging from 180 to 340 µg/l in flow-through measured

tests (Ruesink and Smith, 1975; Adelman and Smith, 1976). This latter comparison indicates that a factor might be required to adjust LC50 values from static or unmeasured tests to comparable values from flow-through measured tests. However, as will be discussed later, the potential effect of pH on the toxicity of PCP renders comparisons between tests questionable unless the pH of the test media is properly monitored.

In the absence of specific data for adjusting static or unmeasured PCP 96-hour LC50 values to measured, flow-through values, the adjustment factors from the Guidelines were used when necessary.

The preponderance of static, unmeasured 96-hour LC50 values for salmonids is probably acceptable because most mortality in PCP tests with salmonids appears to occur within the first 24 to 48 hours, even in flow-through tests (Cardwell, 1976; Webb and Brett, 1973; Chapman and Shumway, 1978). Salmonids appear to be more sensitive to PCP than nonsalmonid species. The range of adjusted 96-hour LC50 values is 20 to 138 (geometric mean 58) µg/l for five species of salmonids and 33 to 340 (geometric mean 180) µg/l for four nonsalmonid species.

For all fish species tested, the adjusted 96-hour LC50 values range from 20 to 340 µg/l and the geometric mean is 96.1 µg/l. Dividing this mean by the species sensitivity factor (3.9) to compensate for 95 percent of overall fish species variability yields a value of 25 µg/l, and the lowest adjusted 96-hour LC50 was 20 µg/l. The similarity of these

two figures indicates that fish species variability with respect to the acute effects of PCP is adequately represented by the sensitivity factor, and that the Final Fish Acute Value of 25 µg/l is a reasonable value.

There are only two studies listed in Table 2 relating the acute toxicity of PCP to invertebrate species. These data are insufficient to determine specific factors for adjusting invertebrate LC50 data, based on static tests, unmeasured concentrations, or shorter than 96-hour tests, to equivalent 96-hour, measured, flow-through test data. The range of adjusted 96-hour LC50 values is 68 to 567 ug/l, which is higher than the range obtained with nine species of fish (20 to 340 µg/l). The geometric mean of the invertebrate values is 290 µg/l. Dividing 290 µg/l by the sensitivity factor (21) results in a Final Invertebrate Acute Value of 14 µg/l, which is lower than the comparable fish value (25 µg/l). Therefore, 14 µg/l becomes the Final Acute Value. These data indicate the invertebrate species are generally similar to fish in sensitivity to the acute toxicity of PCP.

A particularly interesting feature of Table 2 is the indication that the acute toxicity of PCP is pH dependent, becoming more toxic to the tubificid worm with increasing acidity (Whitley, 1968). This is consistent with the frequently demonstrated result that molecular forms of substituted phenols are more toxic than the ionized forms. Thus, at lower pH values more molecular PCP exists than at higher pH values which favor the ionization of PCP into phenate

and hydrogen ions. Unfortunately, no longer-term data on the effects of pH on PCP toxicity are available, and it is inadvisable to extrapolate quantitatively from this single 24-hour test to PCP toxicity in general.

Chronic Toxicity

No data were found to describe the chronic effects of PCP to either fish or invertebrate species.

Plant Effects

Huang and Gloyna (1968) studied the effect of PCP and 40 other substituted phenols and herbicides on chlorophyll destruction and photosynthesis of the alga, Chlorella pyrenoidosa. PCP was by far the most toxic compound tested, producing complete destruction of chlorophyll in 72 hours at 7.5 µg/l (Table 3). No detailed results of the PCP test were given, so it is not possible to fully evaluate this result or determine a general dose-response relationship. Another study of PCP-induced chlorosis in plants (Lemna minor) yielded a 48-hour EC50 of 800 µg/l (Blackman, et al. 1955).

In the absence of additional plant data, it is difficult to assess the relative sensitivity of aquatic plants and animals to PCP, since the 7.5 µg/l plant value is lower than the lowest fish or invertebrate 96-hour LC50 of 20 µg/l and the 800 µg/l plant value is higher than any fish or invertebrate LC50 except the 1,400 ug/l 24-hour LC50 for Tubifex at pH 9.5.

Residues

Two studies were found which provided adequate description of methods to reasonably assure that equilibrium levels

of PCP were attained in the tissues of test organisms (Table 4). Both studies used renewed static PCP concentrations of 100 µg/l.

The data of Kobayashi and Akitake (1975) indicated that equilibrium was attained after 96 hours and that the whole body had a bioconcentration factor of approximately 1,000. The data of Pruitt, et al. (1977) suggested that bioconcentration was maximal after 8 days and declined thereafter. The bioconcentration factor for the muscle was 13 after 8 days. PCP was rapidly lost from the body when the fish were placed in PCP-free water.

Miscellaneous

Additional data regarding the toxicity of PCP to freshwater organisms are listed in Table 5. The most significant results are those on growth and on the effect of pH on toxicity. The data of Crandall and Goodnight (1959) reinforce the previously discussed concept that lower pH values increase the toxicity of PCP. A PCP concentration of 1,000 µg/l was about 50 times more rapidly lethal to guppies at pH 6 than at pH 9.

A number of longer-term studies of 3- to 13-week duration showed that the primary subacute effect of PCP on fish was a reduction in growth rate. Ten studies with salmonid fish yielded growth inhibitions of from 10 to 27 percent at PCP concentrations ranging from 3.5 to 30 µg/l (Webb and Brett, 1973; Chapman, 1969; Chapman and Shumway, 1978; and Matida, et al. 1970).

The 10 percent growth reduction seen by Webb and Brett (1973) was observed at a concentration (3.5 µg/l) which was 6 percent of the 96-hour LC50 (63 µg/l) for the test fish. Using the 6 percent factor with the Final Fish Acute Value of 25 µg/l would result in an estimated growth effect at a PCP concentration of 1.5 µg/l.

CRITERION FORMULATION

Freshwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 25 µg/l

Final Invertebrate Acute Value = 14 µg/l

Final Acute Value = 14 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 7.5 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 7.5 µg/l

0.44 x Final Acute Value = 6.2 µg/l

The absence of chronic toxicity data and the incomplete picture of the effects of pH on the toxicity of PCP render the establishment of a water quality criterion for PCP rather uncertain. A concentration of 1.5 µg/l may inhibit fish growth slightly. In addition, complete chlorosis of algae was reported at 7.5 µg/l.

No freshwater criterion can be derived for pentachlorophenol using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Data for pentachlorophenol and saltwater organisms can be used to estimate a criterion.

For pentachlorophenol and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of a life cycle test with the sheepshead minnow. Therefore, a reasonable estimate of a criterion for pentachlorophenol and freshwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for pentachlorophenol is the Final Acute Value of 14 µg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. A 10 percent reduction in growth of sockeye salmon was observed at a concentration of 3.5 µg/l, a concentration slightly lower than the 24-hour average concentration. It is felt that additional data on adverse effects at these concentrations are needed before lowering the criterion.

CRITERION: For pentachlorophenol the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 6.2 µg/l as a 24-hour average and the concentration should not exceed 14 µg/l at any time.

Table 1. Freshwater fish acute values for pentachlorophenol

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Coho salmon, Oncorhynchus kisutch	S	U	96	96	52	Davis & Hoos, 1975
Coho salmon, Oncorhynchus kisutch	S	U	96	37	20	Davis & Hoos, 1975
Sockeye salmon, Oncorhynchus nerka	S	U	96	50	27	Davis & Hoos, 1975
Sockeye salmon, Oncorhynchus nerka	S	U	96	130	71	Davis & Hoos, 1975
Sockeye salmon, Oncorhynchus nerka	FT	U	96	63	49	Webb & Brett, 1973
Rainbow trout, Salmo gairdneri	S	U	48	170	75	Alabaster, 1957
Rainbow trout, Salmo gairdneri	S	U	96	75	41	Bentley, et al. 1975
Rainbow trout, Salmo gairdneri	S	U	96	92	50	Bentley, et al. 1975
Rainbow trout, Salmo gairdneri	S	U	96	92	50	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S	U	96	96	52	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S	U	96	50	27	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S	U	96	100	55	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S	U	96	48	26	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S	U	96	75	41	Davis & Hoos, 1975
Brown trout, Salmo trutta	S	U	48	170	75	Alabaster, 1957

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Brook trout, Salvelinus fontinalis	FT	M	96	138	138	Cardwell, et al. 1976
Goldfish, Carassius auratus	FT	M	96	210	210	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	220	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	230	230	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	210	210	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	170	170	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	170	170	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	220	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	230	230	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	240	240	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	240	240	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	200	200	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	190	190	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	290	290	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	300	300	Adelman & Smith, 1976

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Goldfish, Carassius auratus	FT	M	96	200	200	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	96	250	250	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	200	200	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	180	180	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	220	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	180	180	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	190	190	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	210	210	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	220	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	180	180	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	190	190	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	190	190	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	240	240	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	200	200	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	200	200	Adelman & Smith, 1976

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Fathead minnow, Pimephales promelas	FT	M	96	190	190	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	270	270	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	230	230	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	96	285	285	Cardwell, et al. 1976
Fathead minnow, Pimephales promelas	S	U	96	600	328	Mattson, et al. 1976
Fathead minnow, Pimephales promelas	FT	M	96	210	210	Ruesink & Smith, 1975
Fathead minnow, Pimephales promelas	FT	M	96	340	340	Ruesink & Smith, 1975
Guppy, Poecilia reticulata	FT	M	96	248	248	Anderson & Weber, 1975
Bluegill, Lepomis macrochirus	S	U	96	60	33	Bentley, et al. 1975
Bluegill, Lepomis macrochirus	S	U	96	77	42	Bentley, et al. 1975
Bluegill, Lepomis macrochirus	S	M	96	260	185	Pruitt, et al. 1977
Bluegill, Lepomis macrochirus	S	M	96	330	234	Pruitt, et al. 1977

*S = static, FT = flow-through

**U = unmeasured, M = measured

Geometric mean of adjusted acute values = 96.1 µg/l $\frac{96.1}{3.9}$ = 25 µg/l

Lowest value from a flow-through test with measured concentration = 138 µg/l

Table 2. Freshwater invertebrate acute values for pentachlorophenol

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Tubificid worm, Tubifex tubifex	S	U	24 pH=7.5	310	68	Whitley, 1968
Tubificid worm, Tubifex tubifex	S	U	24 pH=8.5	670	148	Whitley, 1968
Tubificid worm, Tubifex tubifex	S	U	24 pH=9.5	1,400	308	Whitley, 1968
Cladoceran, Daphnia magna	S	U	48	680	576	U.S.EPA, 1978

* S = static

** U = unmeasured

Geometric mean of adjusted acute values = 290 µg/l $\frac{290}{21}$ = 14 µg/l

Table 3. Freshwater plant effects for pentachlorophenol

Organism	Effect	Concentration (ug/l)	Reference
Alga, *Chlorella pyrenoidosa*	Chlorosis, 72-hr EC100	7.5	Huang & Gloyna, 1968
Duckweed, *Lemna minor*	Chlorosis, 48-hr EC50	800	Blackman, et al. 1955

Lowest plant value = 7.5 µg/l

Table 4. Freshwater residues for pentachlorophenol

Organism	Bioconcentration Factor	Time (days)	Reference
Goldfish, *Carassius auratus*	1,000	5	Kobayashi & Akitake, 1975
Bluegill, *Lepomis macrochirus*	13*	8	Pruitt, et al. 1977

* Muscle tissue.

Table 5. Other freshwater data for pentachlorophenol

Organism	Test Duration	Effect	Result (ug/l)	Reference
Sea lamprey, Petromyzon marinus	4 hrs	LC100	1,000	Applegate, et al. 1957
Sockeye salmon, Oncorhynchus nerka	6 wks	10% growth inhibition	3.5	Webb & Brett, 1973
Rainbow trout, Salmo gairdneri	4 hrs	LC100	1,000	Applegate, et al. 1957
Rainbow trout, Salmo gairdneri	5 days	LC25	100	Chapman, 1969
Rainbow trout, Salmo gairdneri	20 days	11% growth inhibition	30	Chapman, 1969
Rainbow trout, Salmo gairdneri	20 days	18% growth inhibition	30	Chapman, 1969
Rainbow trout, Salmo gairdneri	21 days	19% growth inhibition	30	Chapman, 1969
Rainbow trout, Salmo gairdneri	28 days	12% growth inhibition	30	Chapman, 1969
Rainbow trout, Salmo gairdneri	38 days	18% growth inhibition	30	Chapman, 1969
Rainbow trout, Salmo gairdneri	41 days	LC100	50	Chapman, 1969
Rainbow trout, Salmo gairdneri	41 days	13% growth inhibition	10	Chapman, 1969
Rainbow trout, Salmo gairdneri	92 days	9% growth inhibition	20	Chapman & Shumway, 1978
Rainbow trout, Salmo gairdneri	28 days	27% growth inhibition	8	Matida, et al. 1970
Atlantic salmon, Salmo salar	24 hrs	Altered temperature preference	50	Peterson, 1976
Brook trout, Salvelinus fontinalis	336 hrs	LC50	118	Cardwell, et al. 1976
Goldfish, Carassius auratus	336 hrs	LC50	189	Cardwell, et al. 1976

Table 5. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Fathead minnow, Pimephales promelas	336 hrs	LC50	153	Cardwell, et al. 1976
Guppy, Poecilia reticulata	24 hrs	LC40	360	Crandall & Goodnight, 1959
Guppy, Poecilia reticulata	21-38 mins	LC50 pH = 5.9-6.0	1,000	Crandall & Goodnight, 1959
Guppy, Poecilia reticulata	72-93 mins	LC50 pH = 7.5-7.6	1,000	Crandall & Goodnight, 1959
Guppy, Poecilia reticulata	24 hrs	LC50 pH = 8.9-9.0	1,000	Crandall & Goodnight, 1959
Guppy, Poecilia reticulata	90 days	LC45	500	Crandall & Goodnight, 1959
Bluegill, Lepomis macrochirus	336 hrs	LC50	188	Cardwell, et al. 1976

SALTWATER ORGANISMS

Introduction

Pentachlorophenol (PCP) and its sodium salt (Na-PCP) occur in a wide variety of products that can cause contamination of the saltwater environment. PCP behaves as a weak acid that is readily dissociated to form its corresponding salt in an alkaline solution (Bevenue and Beckman, 1967).

Acute Toxicity

The adjusted 96-hour LC50 values (Table 6) for sheepshead minnows, pinfish and striped mullet ranged from 21 to 442 µg/l (Borthwick and Schimmel, 1978; Parrish, et al. 1978; Schimmel, et al. 1978). The LC50 values based on static tests and unmeasured concentrations were lower than those based on flow-through tests and measured concentrations in tests described in other reports. No significant mortality of the longnose killifish occurred after a 96-hour exposure to 306 µg/l (Table 11) (Schimmel, et al. 1978). The sensitivity of freshwater fishes tested (Table 1) is about the same as that of saltwater fishes.

The unadjusted 96-hour LC50 values in static tests with grass shrimp were 649 µg/l for larvae and 436 µg/l for adults (Borthwick and Schimmel, 1978; Conklin and Rao, 1978). The 96-hour LC50 values using static test conditions for juvenile pink shrimp was 5,600 µg/l (Bentley, et al. 1975). In flow-through tests, Schimmel, et al. (1978) found no significant mortality among juvenile grass shrimp or juvenile brown shrimp after 96-hour exposures to 515 µg/l and 195 µg/l, respectively (Table 11).

Pentachlorophenol appears to be most toxic to molluscs (Tables 7 and 11), which is consistent with the known molluscicidal application of PCP (Bevenue and Beckman, 1967). Most Pacific oyster embryos developed abnormally to the straight-hinged stage when exposed to 55 µg/l for 48 hours (Table 11) (Woelke, 1972), whereas the 48-hour EC50 based on abnormal embryonic development of the Eastern oyster was 40 µg/l (Table 7) (Borthwick and Schimmel, 1978). Also, the 192-hour EC50 based on reduced shell deposition in the Eastern oyster (Schimmel, et al. 1978) was 34 µg/l (Table 11).

The data indicate that shrimp are less sensitive and oysters more sensitive to acute exposures to PCP than are fishes. Freshwater invertebrate species tested were comparably sensitive; however, no freshwater mollusc has been tested (Table 2).

Variability in sensitivity of fishes and particularly invertebrate species exposed to pentachlorophenol is large (Tables 6 and 7). Therefore, use of the greater Guidelines sensitivity factors for invertebrate species rather than for fishes appears justified. When the geometric mean of the adjusted fish LC50 values for PCP is divided by the sensitivity factor of 3.7, a Final Fish Acute Value of 25 µg/l results (Table 6). This value is lower than all but one adjusted LC50 value (for prolarval pinfish) in six tests representing three species. The geometric mean of the adjusted invertebrate LC50 values for PCP, when divided by the species sensitivity factor of 49, gives a Final Invertebrate Acute Value of 8.5 µg/l (Table 7). Since this value is lower

than all adjusted LC50 values for the three species tested, the sensitivity adjustment factor appears adequate. Since the Final Invertebrate Acute Value (8.5 µg/l) is lower than the equivalent value for saltwater fish, it also becomes the Final Acute Value.

Chronic Toxicity

In a 151-day life-cycle exposure with the sheepshead minnow that started with embryos, there was significant mortality of parental fish at a pentachlorophenol concentration of 88 µg/l; 195 µg/l significantly reduced hatching of embryos spawned by parental fish and survival of second generation fish (Table 8) (Parrish, et al. 1978). No statistically significant effect on any portion of the life cycle of this species was observed at a concentration of 47 µg/l. This concentration is about one-tenth of the 96-hour LC50 (442 µg/l) and thus there is relatively little difference between concentrations that are acutely or chronically toxic. In acute tests, pinfish (LC50 values of 38 and 53.2 µg/l) and the Eastern oyster (EC50 value of 40 µg/l) were about ten times more sensitive than was the sheepshead minnow (LC50 value of 442 µg/l); therefore, concentrations that did not affect sheepshead minnows in chronic tests would not protect pinfish or the oysters from either acute of chronic exposure.

Data from a life-cycle exposure of the sheepshead minnow (Parrish, et al. 1978) were used to obtain a fish chronic value of 64 µg/l for pentachlorophenol (Table 8). Use of the species sensitivity factor appears to be justified, since in acute studies with pentachlorophenol the sheepshead

minnow is less sensitive than several other saltwater fishes. Therefore, when the geometric mean of the chronic value is divided by the species sensitivity factor of 6.7, a Final Fish Chronic Value of 9.6 µg/l results (Table 8).

No saltwater invertebrate species has been tested in a chronic toxicity study so the Final Fish Chronic Value becomes the Final Chronic Value.

Plant Effects

Plant values (Table 9) are higner than the chronic values determined for the sheepshead minnow and the 48-hour acute value for the Eastern oyster and most of the 96-hour acute values for fish. Concentrations protective of fishes and invertebrate species for acute toxicity would be expected not to affect saltwater phytoplankton. Exposue to 293 µg/l caused a 58 percent decrease in cell numbers of the alga, Monochrysis lutheri, after 12 days (Woelke, 1965) and exposure to 300 µg/l caused 50 percent inactivation of photosynthesis in kelp, Macrocystis pyrifera, after 4 days (Clendenning and North, 1960). The 72-hour EC50 of a freshwater alga, Chlorella pyrenoidosa, was 7.5 µg/l (Table 3), a concentration lower than the values for saltwater species tested.

Residues

Pentachlorophenol in water was not accumulated appreciably by saltwater fish or invertebrate species (Table 10). The average PCP bioconcentration factors (concentration in tissue divided by concentration in water) for sheepshead minnows were 34 for juveniles after a 28-day exposure and 13 for adults after a 151-day exposure (Parrish, et al. 1978).

Eastern oysters exposed to 25 and 2.5 µg/l for 28 days accumulated the chemical in their tisues to an average of 41 and 78 times, reaching equilibrium in tissues within 4 days, and when held in PCP-free water, depurated the chemical to nondetectable concentrations in 4 days (Schimmel, et al. 1978).

Bioconcentration factors for 96-hour exposures indicate that shrimp bioconcentrate PCP less than do fishes (Table 11). In 96-hour tests, Schimmel, et al (1978) determined bioconcentration factors of 1.7 for grass shrimp and 0.26 for brown shrimp compared to 30 for longnose killifish and 38 for striped mullet.

The absence of a maximum permissible tissue concentration makes it impossible to calculate a Residue Limited Toxicant Concentration.

Miscellaneous

Additional studies indicate that PCP is very toxic to invertebrate species, particularly to molluscs (Table 11). No larvae of the Eastern oyster survived a 14-day exposure to 50 µg/l (Davis and Hidu, 1969). Lugworm, Arenicola cristata, feeding activity was significantly inhibited by 80 µg/l during a 144-hour exposure (Rubinstein, 1978).

Laboratory tests that assess the impact of toxicants that alter the structure of settling benthic communities support the conclusion reached from acute tests, namely, that molluscs are highly sensitive to PCP (Table 11). As little as 7 µg/l decreased the number of molluscs that developed from larvae in unfiltered salt water during a 9-week exposure; 15.8 µg/l significantly decreased the number of

molluscs in a 13-week exposure to a bactericide that contained 79 percent NaPCP (Tagatz, et al. 1977, 1978). In this 13-week study, numbers of polychaete worms, barnacles, amphipods, and meiobenthic nematodes were significantly reduced at 161 µg/l (Tagatz, et al. 1978; Cantelmo and Rao, 1978). Significant reduction in total number of benthic macrofauna occurred in the 9-week exposure of settling communities to 76 µg/l (Tagatz, et al. 1977). No other data from Table 11 suggest any more sensitive effects.

Because the saltwater criterion for pentachlorophenol was derived primarily from LC50 values for shrimp, it may not be protective of oysters and other molluscs. Shrimp were even less sensitive than fishes; the single LC50 value for a mollusc that was used to derive the criterion, together with various other molluscan data not used to derive the criterion indicate that mulluscs are most sensitive to PCP. An invertebrate chronic study, particularly on a mollusc, might also provide a basis for a criterion that would ensure protection of saltwater molluscs.

CRITERION FORMULATION

Saltwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 25 µg/l

Final Invertebrate Acute Value = 8.5 µg/l

Final Acute Value = 8.5 µg/l

Final Fish Chronic Value = 9.6 µg/l

Final Invertebrate Chronic Value = not available

Final Plant Value = 290 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 9.6 µg/l

0.44 x Final Acute Value = 3.7 µg/l

The maximum concentration of pentachlorophenol is the Final Acute Value of 8.5 µg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For pentachlorophenol the criterion to protect saltwater aquatic life as derived using the Guidelines is 3.7 µg/l as a 24-hour average and the concentration should not exceed 8.5 µg/l at any time.

Table 6. Marine fish acute values for pentachlorophenol

Organism	Bioassay Method*	Test Concn*	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Sheepshead minnow (1-day fry), Cyprinodon variegatus	S	U	96	329	180	Borthwick & Schimmel, 1978
Sheepshead minnow (juvenile), Cyprinodon variegatus	S	U	96	223	122	Borthwick & Schimmel, 1978
Sheepshead minnow (juvenile), Cyprinodon variegatus	FT	M	96	442	442	Parrish, et al. 1978
Pinfish (prolarvae), Lagodon rhomboides	S	U	96	38	21	Borthwick & Schimmel, 1978
Pinfish (juvenile), Lagodon rhomboides	FT	M	96	53.2	53.2	Schimmel, et al. 1978
Striped mullet (juvenile), Mugil cephalus	FT	M	96	112.1	112.1	Schimmel, et al. 1978

*S = static; FT = flow-through

**M = measured; U = unmeasured

Geometric mean of adjusted values = 92.78 µg/l $\frac{92.78}{3.7}$ = 25 µg/l

Lowest value from a flow-through test with measured concentrations = 53 µg/l

Table 7. Marine invertebrate acute values for pentachlorophenol

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Eastern oyster (embryo), Crassostrea virginica	S	U	48	40	34	Borthwick & Schimmel, 1978
Grass shrimp (larva), Palaemonetes pugio	S	U	96	649	550	Borthwick & Schimmel, 1978
Grass shrimp (adult), Palaemonetes pugio	S	U	96	436	369	Conklin & Rao, 1978
Pink shrimp (juvenile), Penaeus duorarum	S	U	96	5,600	4,743	Bentley, et al. 1975

* S = static

** U = unmeasured

Geometric mean of adjusted values = 417 ug/l $\frac{417}{49}$ = 8.5 ug/l

Table 8. Marine fish chronic values for pentachlorophenol (Parrish, et al. 1978)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
Sheepshead minnow, Cyprinodon variegatus	LC	47-88	64

*LC = life cycle or partial life cycle

Geometric mean of chronic values = $64\ \mu g/l \frac{64}{6.7} = 9.6\ \mu g/l$

Lowest chronic value = 64 µg/l

Application Factor Values

Species	96-hr LC50 (µg/l)	MATC (µg/l)	AF
Sheepshead minnow, Cyprinodon variegatus	442	47-88	0.145

Geometric mean AF = 0.145

$$0.145 \sqrt{442\ \mu g/l \times 25\ \mu g/l} = 15\ \mu g/l$$

Table 9. Marine plant effects for pentachlorophenol

Organism	Effect	Concentration (ug/l)	Reference
Alga, *Monochrysis lutheri*	58% decrease cell numbers	293	Woelke, 1965
Kelp, *Macrocystis pyrifera*	50% inactivation photosynthesis in 4 days	300	Clendenning & North, 1960

Lowest plant value = 293 µg/l

Table 10. Marine residues for pentachlorophenol

Organism	Bioconcentration Factor	Time (days)	Reference
Eastern oyster (adult), Crassostrea virginica	78	28 days; Equilibrium in 4 days	Schimmel, et al. 1978
Eastern oyster (adult), Crassostrea virginica	41	28 days; Equilibrium in 4 days	Schimmel, et al. 1978
Sheepshead minnow (juvenile), Cyprinodon variegatus	34*	28 days	Parrish, et al. 1978
Sheepshead minnow (adult), Cyprinodon variegatus	13*	151 days	Parrish, et al. 1978

* Average of all concentrations

Table 11. Other marine data for pentachlorophenol

Organism	Test Duration	Effect	Result (ug/l)	Reference
Anemone,	4 days	None survived	1,000	Turner, 1948
Lugworm (adult), Arenicola cristata	144 hrs	Inhibited feeding	80	Rubinstein, 1978
Pacific oyster (embryo), Crassostrea gigas	48 hrs	61.6% embryos abnormal	55	Woelke, 1972
Eastern oyster (embryo), Crassostrea virginica	48 hrs	No eggs developed	250	Davis & Hidu, 1969
Eastern oyster (larva), Crassostrea virginica	14 days	No larvae survived	50	Davis & Hidu, 1969
Eastern oyster (adult), Crassostrea virginica	192 hrs	Reduced shell deposition, EC50	34	Schimmel, et al. 1978
Hard clam (embryo), Mercenaria mercenaria	48 hrs	No eggs developed	250	Davis & Hidu, 1969
Hard clam (larva), Mercenaria mercenaria	12 days	No larvae survived	250	Davis & Hidu, 1969
Bay mussel (larva), Mytilus edulis	--	22.1% abnormal larvae	400	Dimick & Breese, 1965
Mussel	3 days	None survived	1,000	Turner, 1948
Carpet shell, Tapes (=Venerupis) philippinarum	120 hrs	Lethal	100	Tomiyama, et al. 1962
Carpet shell, Tapes philippinarum	24 hrs	Bioconcentration factor about 20	--	Kobayashi, et al. 1969
Barnacle	4 days	None survived	1,000	Turner, 1948
Grass shrimp (juvenile), Palaemonetes pugio	96 hrs	No significant mortality	515	Schimmel, et al. 1978

Table 11. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Grass shrimp (juvenile), Palaemonetes pugio	96 hrs	Bioconcentration factor = 1.7	--	Schimmel, et al. 1978
Grass shrimp (adult), Palaemonetes pugio	9 days	50% reduction in limb regeneration	473	Rao, et al. 1978
Grass shrimp (adult), Palaemonetes pugio	1 hr	Bioconcentration factor = 6.5		Conklin & Rao, 1978
Brown shrimp (juvenile), Penaeus aztecus	96 hrs	No significant mortality	195	Schimmel, et al. 1978
Brown shrimp (juvenile), Penaeus aztecus	96 hrs	Bioconcentration factor = 0.26	--	Schimmel, et al. 1978
Bryozoan, Bugula sp.	1 day	None survived	1,000	Turner, 1948
Meiobenthic nematodes	9 wks	Decrease in biomass and density	622	Cantelmo & Rao, 1978
Meiobenthic nematodes	13 wks	Decrease in biomass and density	161	Cantelmo & Rao, 1978
Benthic macrofauna	9 wks	Significantly reduced number of individuals	76	Tagatz, et al. 1977
Benthic macrofauna	13 wks	Significantly reduced mollusks	15.8	Tagatz, et al. 1978
Benthic macrofauna	13 wks	Significantly reduced arthropods and annelids	161	Tagatz, et al. 1978
Sea grapes, Molgula sp.	1 day	None survived	1,000	Turner, 1948
Longnose killifish (juvenile), Fundulus similis	96 hrs	No significant mortality	306	Schimmel, et al. 1978
Longnose killifish (juvenile), Fundulus similis	96 hrs	Bioconcentration factor = 30	--	Schimmel, et al. 1978

Table 11. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Striped mullet (juvenile), Mugil cephalus	96 hrs	Bioconcentration factor = 38	--	Schimmel, et al. 1978

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Mammalian Toxicology and Human Health Effects

EXPOSURE

Residues of PCP have been found in food, water, and human tissues (Bevenue and Beckman, 1967; Johnson and Manske, 1977; Buhler, et al. 1973; Shafik, 1973; Kutz, et al. 1978). It does not follow, however, that in each instance the total residue results directly from PCP applications. Yang, et al. (1975) suggested the formation of PCP in the rhesus monkey following administration of hexachlorobenzene (HCB). Hexachlorobenzene is a registered pesticide and is used as a fungicide. It is also a frequent contaminant in commercial PCP and chlorinated solvents. HCB is the most commonly found chlorinated hydrocarbon in meat (Conklin and Fox, 1978). Consequently, the degradation of HCB to PCP may account for part of the PCP residue present in certain commodities. Lui and Sweeney (1975) and Mehendale, et al. (1975) reported the isolation of PCP from the urine of rats which had been dosed with HCB. Microsomal preparations from rat liver were able to produce one or more chlorophenols including PCP from HCB (Mehendale, et al. 1975). Koss and Koransky (1978) administered labeled HCB to rats and collected urine and feces for 4 weeks. HCB was metabolized to PCP, tetrachlorohydroquinone and pentachlorothiophenol. Twenty-eight percent of the HCB was recovered as PCP in the urine and 16 percent as PCP in the feces. These results suggest that metabolism of HCB to PCP can be a significant consideration. Karapally, et al. (1973) obtained tentative gas chromatographic identification of PCP in the urine of rabbits

receiving ^{14}C-labeled lindane (y-1,2,3,4,5,6-hexachlorocyclohexame). Rats given 8 mg HCB/kg for 19 days had tissue residues of HCB and metabolites consisting of PCP, small amounts of 2,3,4,6-tetrachlorophenol, 2,3,5,6-tetrachlorophenol, 2,4,6-trichlorophenol and pentachlorobenzene (Engst, et al. 1976a). PCP, tetrachlorophenol and trichlorophenols are also metabolites of lindane in the rat (Engst, et al. 1976b). Lindane applied to lettuce growing outdoors degraded to free trichlorophenol, 2,3,4,6-tetrachlorophenol, pentachlorophenol, conjugates of the latter two compounds and unidentified water-soluble products (Kohli, et al. 1976).

The results of these studies suggest several possible sources for the residues of PCP in foods and tissues, in addition to residues resulting from the direct use of PCP.

Ingestion from Food and Water

Pentachlorophenol is absorbed from the digestive tract. Pentachlorophenol was detected in 13 of 240 food composites collected from August 1974 to July 1975 at levels of 0.01 to 0.04 mg/kg (Johnson and Manske, 1977). The highest residue (0.04 mg/kg) was reported in the food category of sugars and adjuncts.

Buhler, et al. (1973) reported pentachlorophenol levels of 0.06 µg/l in finished drinking water prepared from raw water containing 0.17 µg/l. The calculated daily dietary exposure is 1 to 6 µg/person/day (Duggan and Corneliussen, 1972).

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

Measured steady-state bioconcentration factors were obtained for pentachlorophenol using four species:

Organisms	BCF	Percent Lipids	Adjusted BCF	Reference
Goldfish, *Carassius auratus*	1,000	8	290	Kobayashi & Akitake, 1975
Bluegill, *Lepomis macrochirus*	13	1	30	Pruitt, et al. 1977
Eastern oyster (adult), *Crassostrea virginica*	78	1	180	Schimmel, et al. 1978
Eastern oyster (adult), *Crassostrea virginica*	41	1	94	Schimmel, et al. 1978
Speepshead minnow (juvenile), *Cyprinodon variegatus*	34	5	16	Parrish, et al. 1978
Sheepshead minnow (adult), *Cyprinodon variegatus*	13	5	6	Parrish, et al. 1978

Each of these measured BCF's was adjusted from the percent lipids of the test species to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. The geometric mean was obtained for each species, as was the geometric mean for all species. Thus the weighted average bioconcentration factor for pentachlorophenol and the edible portion of all aquatic organisms consumed by Americans is calculated to be 58.

Inhalation

Inhalation exposure data for the general population are not available. However, some exposure data and criteria are available for industrial situations. The threshold limit value is 0.5 mg/m^3 and levels greater than 1.0 mg/m^3 cause respiratory irritation in unacclimated persons (American Industrial Hygiene Association, 1970). This value provides a moderate margin of safety for an 8 hr/day, 5 day/week exposure.

Wyllie, et al. (1975) sampled air 5 times at 11 sites in a plant treating 2.5 million board feet of lumber annually. Average air PCP levels ranged from 0.263 to 1.888 $\mu g/m^3$. The highest PCP level reported was 15 $\mu g/m^3$ in an air sample from the pressure treating room. The air samples were collected for an average of six hours. Air PCP levels in storage areas ranged from 0.009 to 9.0 $\mu g/m^3$. Serum PCP levels in six workers were 1-2 mg/L. Urine PCP levels were 0.08-0.3 mg/L. The highest serum PCP level was 3.9 mg/L. PCP levels in the one control reported were 0.04-0.07 mg/L in serum and 0.002-0.004 mg/L in urine.

The resulting inhalation exposure can be estimated using the above maximum air level of 15 $\mu g/m^3$ as follows. With an average minute respiratory volume of 26 L/minute, approximately 4 times resting volume, a worker would inhale 12 m^3 of air during an eight hour work period. This ventilation rate includes hard work periods as well as less strenuous activity and rest. Because there is no reliable information available on the pulmonary deposition of PCP vapor

or particles, the inhalation dose calculations assume 100 percent deposition and retention. The resulting pentachlorophenol exposure at an air level of 15 $\mu g/m^3$ is 0.180 mg/person/day. For a 70 kg individual the resulting exposure rate is 0.0025 mg/kg/day. Under steady state conditions the same amount of chemical will be excreted per day as is taken in. Assuming a daily urinary void of 1.4 L/day, the predicted urine level from the air exposure level above would be 0.180 mg $\div$ 1.5 L = 0.13 mg/L. The resulting value of 0.13 mg/L falls between the observed urine levels of 0.08 to 0.3 mg/L reported by Wyllie, et al. (1975). Consequently, all of the inhalation exposure can be accounted for by the PCP levels in the urine. At the same time, since the calculations maximized inhalation doses and the range of urine values actually measured exceeded the calculated urine level, it is reasonable to assume that there was also exposure from oral or dermal routes.

Measured air and urine PCP levels associated with 3 types of wood treating operations in an Oregon wood treating plant are shown in Table 1 (Arsenault, 1976). The maximum air level of 0.297 mg/m^3 (Table 1) is higher than the 0.015 mg/m^3 maximum level reported by Wyllie, et al. (1975).

TABLE 1

Air and Urine PCP Concentration from Plants and Mill Workers in Oregon.

	Air Level - mg/m^3		Urine - mg/L	
Operation	Average	Maximum	Average	Range
Dip	0.019	0.019	2.83	0.12 - 9.68
Spray	0.006	0.026	0.98	0.09 - 2.58
Pressure	0.014	0.297	1.24	1.24 - 5.57

The above data can be used to estimate inhalation exposure (Table 2). The assumptions used include: resting minute respiratory volume (tidal volume times respiratory rate) = 6 L, moderate exercise minute respiratory volume = 24 L, and heavy exercise minute respiratory volume = 100 L; pulmonary deposition and retention of 100 percent; 70 kg person; eight hour exposure.

The important variable in this approach to estimating exposure is the amount of air inhaled which is directly related to the amount of muscular work. It is unlikely that a typical worker is represented by either the resting or heavy exercise breathing rates for the entire 8-hour work period. Consequently, a reasonable assumption would be to use the moderate exercise values which represent respiratory values equal to four times the resting rates.

TABLE 2
Estimated Exposures in $mg/kg\ day^{-1}$ Reported Air PCP Levels

Condition	Resting	Moderate Exercise	Heavy Exercise
	Condition and Minute Respiratory Volume		
Minute respiratory volume:	6 L/min	24 L/min	100 L/min
m^3 air/8 hour	2.88 m^3	11.52 m^3	48 m^3
Air Level:			
0.006 mg/m^3	0.00025 mg/kg	0.001 mg/kg	.0041 mg/kg
0.014 mg/m^3	0.00058	0.0023	0.00958
0.015 mg/m^3	0.00062	0.0025	0.0103
0.019 mg/m^3	0.00078	0.0031	0.0130
0.026 mg/m^3	0.00110	0.0043	0.0178
0.297 mg/m^3	0.0122	0.0489	0.2037

The next step is to compare total inhalation exposure with the amount of PCP found in the urine in the study reported by Arsenault (1976). For the dip treaters, the average urine value of 2.83 mg/L divided by the assumed daily urine volume of 1.4 L results in a total exposure of 3.96 mg PCP/person. The corresponding inhalation exposure assumes moderate exercise and average air level of 0.019 mg/m^3 is 0.0031 mg/kg or 0.217 mg/person. In this instance, inhalation accounts for 5.5 percent of the dose for workers in a dipping operation. The pressure treaters had an average urine level of 1.24 mg/L which results in an estimated total exposure of 1.74 mg/person. The average air level of 0.014 mg/m^3 yields an inhalation exposure of 0.0023 mg/kg or 0.16 mg/person. The resulting estimated inhaled dose is 9 percent of the calculated total body dose.

In a simple 2 subject inhalation trial, 76-88 percent of a calculated respired dose was eliminated within 7 days. Peak urine PCP levels occurred within 48 hours post-exposure (Casarett, et al. 1969).

Dermal

Pentachlorophenol can be absorbed through the intact skin. Pentachlorophenol dissolved in oil solvents has an acute dermal lethal dose of 60-200 mg/kg in rabbits (Deichmann, et al. 1942). Quantitative dermal absorption data for man are not available.

While it is not possible to separate oral, respiratory and dermal exposures, except experimentally, it is possible to establish estimates of total body exposures. Pentachloro-

phenol is primarily excreted in the urine and has a half-life in man of 1.25 days. After 9 days of exposure, an uptake-elimination equilibrium is reached (Braun, et al. 1978). Therefore, the urine PCP concentration can be used to estimate total body exposure. The accuracy of the calculations is limited by the care with which urine samples were collected. The most useful data would be based on 24-hour urine collections, or on levels reported based on mOsmols of urine solute. In absence of these data, the urine levels may range by a factor of 2-3 in either direction depending on volume of fluid intake, sweating, and presence or absence of renal tubular disease. Even with these restrictions the calculated exposures are of value in estimating the probable exposure magnitude. The calculated exposures in Table 4 assume a daily urine volume of 1.4 L for a 70 kg adult steady state conditions and 90 percent elimination of the dose in urine and 10 percent in feces. In addition to the studies on occupational exposures cited above, Kutz, et al. (1978) found an arithmetic average of 6.3 µg/PCP/L in 354 of 418 urine samples (84.0 percent) analyzed. Cranmer and Freal (1970) reported urine levels ranging from 2 to 11 µg/L for general population in a small number of samples.

Exposure estimates, based on reported urine PCP levels, are given in Table 3. These represent total body exposures from all sources and routes.

TABLE 3

Estimated Total Body PCP Exposures for a 70 kg Person Based on Reported Urine PCP Levels and Assumed Daily Urine Void of 1.4L with 90% Urinary Excretion

Urine Level (mg/L)	Reference	Estimated Exposure mg/person day^{-1}	mg/kg day^{-1}
0.0063	Kutz, et al. 1978	0.0098	0.00014
0.011	Cranmer and Freal, 1970	0.017	0.00024
2.83	Arsenault, 1976	4.40	0.0629
0.98	" "	1.52	0.0218
1.24	" "	1.93	0.0276
2.6	Casarett, et al. 1969	4.04	0.0578
1.6	" "	2.49	0.0356

Duggan and Corneluissen (1972), using dietary levels, calculated daily exposures of 0.001-0.006 mg PCP/person day^{-1}. Using the reported urine values and calculated exposures in Table 3, the exposure appears to be in the range of 0.010-0.017 mg/person day^{-1} for the general population and 1.5-4.4 mg for occupational exposures.

PHARMACOKINETICS

Absorption

The pharmacokinetics characteristics for PCP are summarized in Table 4.

The half-life for absorption in man after ingestion is 1.3 $\pm$ 0.4 hr and the peak plasma concentration occurs four hours after ingestion. A 0.1 mg/kg dose results in a peak plasma level of 0.248 mg/L. The calculated 99 percent of steady-state value is 0.491 mg/L which would be reached after 8.4 days of ingestion of 0.1 mg/kg/day^{-1} (Braun, et al. 1978).

TABLE 4

Comparison of PCP Biotransformation in Mammals

SPECIES AND REFERENCE	DOSE & ROUTE	PEAK BLOOD LEVEL	TIME TO PEAK LEVEL	PLASMA HALF-LIFE	EXCRETION IN URINE AND FECES	METABOLITES FOUND, comments
Man, Braun, et al. (1977)	0.1mg/kg Oral	0.248ppm	4 hrs	30.2 hr	Peak at 42 hours half-life for PCP was 33 hours, half-life for PCP glucuronide was 12.7 hours.	74% in urine as PCP-12% in urine as PCP glucuronide- 4% in feces as PCP and PCP glucuronide.
Rat, Braun, et al. (1977)	10mg/kg Male Oral	45ppm	4-6 hrs		80% in urine - 19% in feces	Excretion kinetics: total body half-life males: d=17 hr, B=40 hr. Females: d=13 hr, B=33 hr.
	10mg/kg Female Oral	45ppm	4-6 hrs		78% in urine 19% in feces	
	100mg/kg Male Oral			13 hr - Alpha 121 hr - Beta	72% in urine 24% in feces	Urine - 75% as PCP - 9% as PCP-glucuronide- 16% as tetrachlorohydroquinone(TCH)-half-lives were 24 hr for PCP, 25 hrs for PCP-glucuronide and 32 hrs for TCH.
	100mg/kg Female Oral			27 hr - Alpha No D- Beta	54% in urine 43% in feces	See 100 mg/kg male data above - Urine was pooled
Monkey, Braun and Sauerhoff (1976)	10mg/kg Male Oral	10-30 ppm	12-24 hr	72 hr	Urine half-life 41 hrs	In urine as unchanged PCP; No metabolites.
	10mg/kg Female	10-30 ppm	12-24 hr	83 hr	Urine half-life 92 hours - 360 hours after single dose: 70% in urine, 18% in feces and 11% remained in tissues.	

SPECIES AND REFERENCE	DOSE & ROUTE	PEAK BLOOD LEVEL	TIME TO PEAK LEVEL	PLASMA HALF-LIFE	EXCRETION IN URINE AND FECES	METABOLITES FOUND, comments
Mouse, Jakobson and Yllner (1971)	15-37mg/kg I.P. or S.C.	NR	NR	NR	72-83% excreted in urine in 4 days. About half in 24 hrs. 5-7% in feces.	About 45% as unchanged PCP, 14% as PCP conjugate and 40% as TCH.
Rat, Ahlborg, et al. (1974)	25mg/kg I.P.	NR	NR	NR	70% in urine in 24 hours.	43% as unchanged PCP - 5% as TCH, 38% as TCH conjugate and 14% as PCP conjugate.
Mouse, Ahlborg, et al. (1974)	25mg/kg	NR	NR	NR	70% in urine in 24 hours.	41% as unchanged PCP - 24% as TCH. 22% as TCH conjugate - 13% as PCP conjugate.

FOOTNOTES:

NR - Not reported
TCH - Tetrachlorohydroquinone
IP - Intraperitoneal
SC - Subcutaneous

Braun and Sauerhoff (1976) administered a single oral dose of 10 mg PCP/kg in corn oil to 3 male and 3 female Rhesus monkeys. The half-lives for absorption were 3.6 hours (male) and 1.8 hours (females). Monkeys given a single dose of 10 mg PCP/kg attained peak plasma levels of 10-30 ppm in 12-24 hours. Rats administered single oral doses of 10 mg/kg had peak plasma concentrations of 30-40 ppm in 4-6 hours (Braun, et al. 1977).

Distribution

The quantity of PCP in fat has been investigated in many studies. Larsen, et al. (1975) examined the tissue distribution of PCP in rats following oral administration and found low levels in fat relative to other tissues.

Braun and Sauerhoff (1976) recovered 11.7 and 11.2 percent of the 10 mg/kg dose in the tissues of 2 female monkeys, respectively, 360 hours after administration. The largest amount was found in liver and small and large intestines combined (Table 5). All of the other tissues including brain, fat, muscle, bone and remaining soft tissues contained only 2-3.5 percent of the dose. In summary, 68-83 percent of the residue was in the liver and intestine.

In rats, 9 days after a single 10 mg/kg dose, 0.44 percent of the dose remained in the body with 82 percent of the residue located in the liver and kidney (Braun, et al. 1977). In a study using 1 male and 1 female rat necropsied at each of 4, 24, 48, 72 and 120 hours post-dosing, the highest levels among 10 selected tissues were found in liver and kidney. The lowest levels were found in brain,

spleen and fat. Except for liver in female rats and liver and kidney for male rats, the plasma PCP levels were higher than organ levels.

TABLE 5

Tissue Concentrations of ^{14}C Activity in Two Female Monkeys Administered 10 mg ^{14}C PCP/kg.
(From Braun and Sauerhoff, 1976, p. 530)

Tissue	Percentage of Dose	
	Female 1	Female 2
Liver	1.38	0.81
Small Intestine	7.06	2.94
Large Intestine	1.28	3.91
Other[a]	1.98	3.54
TOTAL	11.7	11.2

[a]Other tissues = adrenals, brain, gall bladder, kidney, lung, ovaries, pancreas, spleen, stomach, urinary bladder, uterus, vagina, heart, bone, skin, fat, muscle, meat, carcass.

A study of blood and urine PCP concentrations of occupationally exposed individuals by Casarett, et al. (1969) suggests a ratio of plasma to urine PCP concentrations of 1.5 to 2.5. The serum to urine PCP concentration ratios in the Wyllie, et al. (1975) study averaged 0.75 for the 6 workers studied. Reported cases of acute intoxications frequently present higher PCP concentrations in the urine than in the plasma. Animal studies with a single dose also show this pattern. Plasma and urine PCP concentrations were linearly related up to about 1.0 mg/L and above 1.0

mg/L the plasma levels reached a plateau approaching 10 mg/L with increasing levels of PCP in the urine.

Data for tissue distribution following uptake of PCP by man is derived mainly from autopsy results of fatal cases of PCP intoxication (Mason, et al. 1965; Gordon, 1956; Armstrong, et al. 1969). Cretney (1976) reported PCP residues from a suicide as: blood 173 mg/L; urine 75 mg/L; liver 225 mg/kg; and kidney 116 mg/kg. From available data levels associated with acute lethal toxicosis can be estimated. Levels in blood, liver and kidney are most meaningful. Levels in urine can be variable, depending on how much urine was in the bladder at the time of ingestion. Residues associated with acute toxicosis and death are: blood, 50-176 mg/L; liver, 62-225 mg/kg; and kidney, 28-123 mg/kg.

Armstrong, et al. (1969) reported analysis of fat tissue from a PCP exposure in an infant exposed to a lethal concentration of Na-PCP in diapers and hospital linen. Residues were: kidney, 2.8 mg/kg; adrenal, 2.7 mg/kg; heart and blood vessel, 2.1 mg/kg; and fat, 3.4 mg/kg. Shafik (1973) found an average of 26.3 micrograms PCP/kg in 18 human fat samples of unspecified origin.

Metabolism

Braun, et al. (1978) determined the metabolism and pharmacokinetics of PCP in 4 male volunteers ingesting 0.1 mg PCP/kg. Approximately 74 percent of the dose was eliminated in the urine as PCP and 12 percent was eliminated in urine as PCP glucuronide. Additionally, 4 percent was eliminated in feces as PCP and PCP glucuronide.

PCP in mice is detoxified by conjugation and metabolism (Jakobsen and Yllner, 1971). Approximately 21 percent of the injected ^{14}C activity was found to consist of ^{14}C-labeled tetrachlorohydroquinone (TCH) which was possibly conjugated in the urine. Rats excrete 75 percent of the PCP in the urine as unchanged PCP, 16 percent as TCH and 9 percent ad PCP-glucuronide (Braun, et al. 1977). In the plasma most of the PCP is unchanged with a small amount of PCP-glucuronide present. TCH was not detected in rat blood plasma.

Ahlborg (1978) found that rats dechlorinate PCP to form TCH and trichloro-p-hydroquinone, but not tetrachlorophenol or trichlorophenol. Ahlborg found the TCH to be conjugated in the urine while Braun, et al. (1977) reported TCH was unconjugated in their study. The rhesus monkey eliminates PCP unchanged in the urine with no metabolites detected (Braun and Sauerhoff, 1976).

Excretion

In man and experimental animals the primary mode of excretion for PCP is urinary (Deichmann, et al. 1942; Jakobsen and Yllner, 1971; Larsen, et al. 1975; Braun, et al. 1978).

In man the plasma PCP half-life is 30.2±4.0 hours. The half-lives for elimination of PCP and PCP glucuronide from urine are 33.1±4.5 hr and 12.7±5.4 hr, respectively. The dynamics of elimination in man are described by a one-compartment open-system model with first-order absorption, enterohepatic circulation and first order elimination (Braun, et al. 1978).

The monkey eliminated PCP more slowly than other animals. In two monkeys 360 hours after a single oral dose of 10 mg/kg, 70 percent of the dose was eliminated in the urine, 18 percent in the feces and 11 percent remained in the carcass. Excretion by the kidney was a first order process characterized by half-lives of 40.8 hr (males) and 92.4 hr (females). Plasma levels decreased by a first order process with half-lives of 72 hr (males) and 83.5 hr (females) (Braun and Sauerhoff, 1976).

Because the Rhesus monkey does not metabolize PCP, it is not a good animal model for man. The pharmacokinetics of PCP in rats given oral doses of 10 mg/kg are summarized in Table 6 (Braun, et al. 1977). The rat eliminates PCP more rapidly than the monkey and appears to be more similar to man.

TABLE 6

Pharmacokinetics of PCP in Rats Given Single Oral Dose of 10 mg/kg

Parameter	Males	Females
K_e (hr^{-1})	0.0343	0.0478
K_{12} (hr^{-1})	0.0046	0.0032
K_{21} (hr^{-1})	0.0061	0.0100
α (hr^{-1})	0.0398	0.0518
β (hr^{-1})	0.0173	0.0213
$t_{1/2}$ (α) (hr)	17.4	13.4
$t_{1/2}$ (β) (hr)	40.2	32.5
V_1 (ml/kg)	136	127

It is difficult to draw reliable conclusions from most of the previously reported human urinary excretion data, except for the Braun, et al. (1978) study, for the following reasons: 1) the exposures were accidental or occupational with the quantity unknown; and 2) the reports do not account for continued background exposure.

There is speculation that there may be long-term accumulation and storage of PCP. This has resulted from consideration of the long-term fat storage of chlorinated hydrocarbon insecticides such as DDT and dieldrin and the inference is made that PCP may act accordingly. The other factor generating this speculation is data from occupationally exposed individuals whose urine or blood PCP levels do not return to zero. This is not unexpected since the control populations studied also have non-zero blood and urine levels. Additionally, none of the studies attempted either to control or to determine the presence of continuing exposure (Bevenue, et al. 1967b). The available literature indicates that PCP does not accumulate in body tissues to any significant extent. Long term, low level tissue binding has not been adequately studied.

EFFECTS

Acute, Sub-acute and Chronic Toxicity

Pentachlorophenol solutions can cause skin irritation. Immersion of hands for 10 minutes in a 0.4 percent solution of PCP can cause pain and inflammation (Bevenue, et al. 1967a).

Dust and mist concentrations greater than 1.0 mg/m^3 cause painful irritation in the upper respiratory tract of persons newly-exposed to PCP which is accompanied by violent sneezing and coughing. Concentrations as high as 2.4 mg/m^3 can be tolerated by conditioned individuals (American Industrial Hygiene Association, 1970).

The oral lethal dose of pentachlorophenol in several species of animals ranges from 70 to 300 mg/kg (Bevenue and Beckman, 1967; Deichmann, et al. 1943). Fuel oil type solvents reduce the lethal dose, while aqueous solutions of the sodium salt are less toxic. The mechanism of action involves the uncoupling of oxidative phosphorylation (Weinbach and Garbus, 1965).

Pentachlorophenol exposure has resulted in death in man through occupational and accidental exposures and suicide attempts (Gordon, 1956; Bergner, et al. 1965; Armstrong, et al. 1969). Symptoms following fatal exposures include general weakness, fatigue, dizziness, headache, anorexia, profuse sweating, nausea, vomiting, hyperpyrexia of 106-108 degrees F, dypsnea, tachycardia, abdominal pain, terminal spasms and death 3-25 hours after onset of symptons. Lesions include inflammed gastric mucosa, pulmonary congestion, pulmonary edema, fatty metamorphosis of the liver, and degeneration of renal tubules and myocardium.

Non-fatal acute exposure can result in skin irritation, nasal and respiratory tract irritation, sneezing and coughing, and eye irritation.

One unique poisoning episode involved babies wearing diapers rinsed in an antimicrobial laundry neutralizer con-

taining sodium pentachlorophenate. Babies wearing the diapers an average of 8 days became ill and some died. Some were less severely affected and recovered spontaneously (Armstrong, et al. 1969; Robson, et al. 1969). Six of the 9 severely affected had hepatomegaly and 2 of the 9 splenomegaly in addition to profuse sweating hyperpyrexia.

A review of the U.S. EPA Pesticide Episode Response Branch report of September 14, 1976, reveals 47 cases of human exposures ranging from direct eye contact to more serious intoxications involving systemic effects. Significant cases include 5 situations where PCP was used inside of homes and resulted in adverse health effects of headache, eye irritation, dyspnea, malaise and in 1 case, chronic weight loss.

One chronic health effect associated some years ago with certain types of commercial PCP is chloracne. Chloracne is a type of acneform dermatitis that looks similar to juvenile acne. It is characterized by folliculitis and comedones with secondary infections. Chloracne results from exposure to a variety of substances including chlorinated biphenyls, chlorinated naphthalenes and tetra- and hexachlorodioxins. Baader and Bauer (1951) reported acne and skin and respiratory tract irritation in workers in a German plant producing PCP from hexachlorobenzene. In addition, 8 of 10 workers reported pain of the lower extremities that occurred with the onset of the chloracne. Nomura (1953) reported 2 cases of acne-form skin eruptions in workers in a PCP plant in Japan. It was not reported whether the PCP was produced from HCB or by the chlorination of phenol.

Johnson, et al. (1973) found that commercial PCP containing higher levels of chlorodioxins produced chloracne in the rabbit ear test. Using pure PCP or PCP with reduced dioxin content did not cause chloracne.

Symptoms in chronic toxicity, in general, are similar to those seen in acute intoxications. Pentachlorophenol does not accumulate in body tissues to the extent of the chlorinated hydrocarbon insecticides DDT and dieldrin. Consequently, chronic intoxications result from relatively high levels of continuous exposure. Symptoms in non-fatal chronic exposures include muscle weakness, headache, anorexia, abdominal pain, and weight loss in addition to skin, eye and respiratory tract irritation.

A group of wood treaters in Hawaii has been studied medically for a number of years. Physiopathologic changes observed have been minimal. Klemmer (1972) noted that serum enzymes SGOT, SGPT, and LDH were highest in the occupationally exposed group but were within normal limits.

Workers chronically exposed to PCP demonstrated significantly elevated levels of total bilirubin and creatinine phosphokinase, although the levels were within normal limits. Workers chronically exposed to PCP showed a significantly higher prevalence of gamma mobility C-reactive protein (CRP) in the sera. The clinical significance of these elevated levels of CRP in individuals exposed to PCP is not known. CRP levels are often elevated in acute states of various inflammatory disorders or tissue damage (Takahashi, et al. 1976).

Begley, et al. (1977) determined plasma and urine PCP and renal creatinine and phosphorus clearance and phosphorus reabsorption in 19 workers before and after a 20-day vacation. Plasma PCP decreased from 5.14 to 2.19 mg/L. Following vacation, both the depressed creatinine clearance values and the phosphorus reabsorption values improved.

Caution is required in interpreting the human epidemiological data since some of the occupationally exposed group were exposed to other wood preserving chemicals and solvents.

Chronic animal studies have been reported which aid in the evaluation of long term health effects. One complicating factor is the presence of varying amounts of non-phenolic contaminants in the pentachlorophenol used in the various studies. Some of the effects are related to the non-phenolic constitutents. Oral doses of 1 and 3 mg technical PCP/kg for 90 days did not produce signs of intoxication in rabbits (Machle, et al. 1943).

Male and female rats fed 25 ppm technical PCP (equivalent to 1.5 mg/kg) for 12 weeks did not show toxicologically significant changes. A level of 50 ppm (approximately 3 mg/kg) resulted in decreased hemoglobin and RBC numbers in male but not female rats. A level of 200 ppm (approximately 14 mg/kg) increased liver aniline hydroxylase activity in male and female rats and decreased hemoglobin and RBC numbers in male rats (Knudsen, et al. 1974).

Goldstein, et al. (1977) fed rats 20, 100 or 500 ppm PCP (equivalent to 1.2, 6 and 30 mg/kg) for 8 months. At 20 ppm, liver aryl hydrocarbon hydroxylase and glucuronyl

transferase were increased in female rats fed technical PCP as compared to controls fed pure PCP. At 100 ppm technical PCP increased excretion of uroporphyrin and delta aminolevulinic acid. Feeding 20 or 100 ppm of pure PCP had no effect. Body weight gain was reduced at 500 ppm with both types of PCP. The no-observable effect level (NOEL) for pure PCP from this study was 6 mg/kg (i.e., the 100 ppm diet group).

To compare the toxicity of pure versus technical PCP, rats were fed the different PCPs for 90 days at levels of 3, 10 and 30 mg/kg (Kociba, et al. 1971; Johnson, et al. 1973). No toxicologic effects were noted in the 3 and 10 mg/kg groups fed pure PCP. There was a relative increase in liver weight at 10 mg/kg. In the technical PCP group the significant effects at 3 mg/kg were an equivocal increase in alkaline phosphatase and increases in relative liver and kidney weights. The alkaline phosphatase activity was increased at 3 and 30 mg/kg but unchanged at 10 mg/kg. Knudsen, et al. (1974) did not find changes in alkaline phosphatase at any dose in either males or females. Histopathologic changes were observed only in the 30 mg/kg technical PCP group and consisted of minimal focal hepatocellular degeneration and necrosis.

Kociba, et al. (1973) fed rats 1, 3, 10 or 30 mg/kg of a low nonphenolic content PCP for 90 days. The no-effect level was 10 mg/kg in females and 3 mg/kg in males. The effect in males at 10 mg/kg was limited to a change in liver weight. There were no treatment-related histopathologic changes.

The NOEL in Sprague-Dawley rats fed a low nonphenolic content PCP for 22-24 months was 3 mg/kg in females and 10 mg/kg in males (Schwetz, et al. 1978). The feeding levels were 1, 3, 10 or 30 mg/kg. The high dose resulted in decreased body weight gain, increased SGPT and increased urine specific gravity. The high dose (30 mg/kg) is 1/5 of the single acute lethal dose of 150 mg/kg for the PCP used in the study. This further points out the lack of significant cumulative effects of PCP even at high dosages.

Teratogenicity

Information on teratogenic studies is limited. No information was encountered suggesting pentachlorophenol is a human teratogen.

Hinkle (1973) found fetal deaths and/or resorptions in 3 of 6 test groups using Golden Syrian Hamsters. Dose-response data and statistical analysis were not provided. Dose range was 1.25 to 20 mg/kg.

A single 60 mg/kg dose on day 9 or 10 reduced fetal weights in Charles River CD strain rats and had no effect when given on days 11, 12 or 13. A total of 4 abnormalities out of 97 fetuses were found. One of 46 fetuses from day 8 exposure was a dwarf and 3 of 51 fetuses from day 9 exposure had different malformations consisting of exencephaly, macropthalmia and taillessness. No skeletal abnormalities were found. An increase in maternal deep body temperature of 0.5 to 0.8 degrees C was reported which indicates systemic toxicity. A dose of 60 mg/kg is about 75 percent of the

LD_{50}. The authors concluded that the number of malformations was minimal and could have been due to toxic effects on the maternal rat (Larsen, et al. 1975).

Schwetz, et al. (1974) provided more complete data from a rat study using purified and commercial grade PCP. Dosages ranged from 5 to 50 mg/kg daily and exposure was during days 6-15 inclusive. The NOEL on incidence of fetal resorption was 5.8 mg/kg for commercial and 15 mg/kg for purified grade PCP. At 50 mg/kg resorption was 100 percent. The NOEL level for reducing fetal body weight was 15 mg/kg for both grades. Fetal anomalies consisting of subcutaneous edema and dilated ureters were observed in soft tissues at doses of 15 mg/kg or above for both grades of PCP. The NOEL for soft tissue anomalies was 5 mg/kg. Delayed ossification of the skull was noted at 5 mg/kg with purified PCP. The NOEL for skeletal anomalies with commercial PCP was 5.8 mg/kg. At higher dosages skeletal anomalies consisted of lumbar spurs; supernumerary or fused ribs; or supernumerary, abnormal shaped, missing or unfused centers of ossification of vertebra or sternebrae. These effects were more readily produced when dosing occurred on days 8-11 rather than days 12-15 of gestation. The authors considered the effects to be evidence of embryotoxicity and fetotoxicity, not teratogenicity. The results were concluded to be due to PCP.

Schwetz, et al. (1978) also reported a reproduction study. Male and female rats were fed 0, 3, or 30 mg PCP/kg for 62 days before mating, during 15 days of mating and

during gestation and lactation. No evidence of toxicosis in the males was reported. The females on the high dose gained less weight. The 3 mg/kg dose was the NOEL. At 30 mg/kg the following indices were decreased: percent liveborn pups; 7, 14, 21 day survival; 1, 7, 14, 21 day body weight-pups, and 7, 14, 21 day litter size. Skeletal abnormalities similar to those in the Schwetz, et al. (1974) study were observed. Since the LD_{50} of PCP in 3 to 4-day-old rats is 65 mg/kg compared to 150 mg/kg in adults, the observed effects on offspring may be the result of fetal toxicity.

Mutagenicity

Sodium PCP was not mutagenic to male germ cells of Drosophila when tested at a concentration of 7 mM (Vogel and Chandler, 1974). PCP was not mutagenic in the mouse host-mediated assay or in in vitro spot tests (Buselmaier, et al. 1973).

Anderson, et al. (1972) also reported that PCP did not produce mutagenic effects when tested in vitro using histidine-requiring mutants of Salmonella typhimurium as the test organism. The purity of the PCP used in the 3 studies cited was not specified.

Fahrig, et al. (1978) tested recrystallized PCP in 2 mutagenic test systems. The first system used Saccharomyces cerevisiae. The PCP concentration used was 400 mg/L which resulted in a 59 percent survival of test organisms and increased frequency of mutations and mitotic gene conversion compared to controls. The second system examined changes

in hair coat color (spots) in mice by injecting dams on the tenth day of gestation with an intraperitoneal dose of either 50 or 100 mg/kg. Four out of 473 offspring were reported to have spots of genetic relevance. In both of the test systems the dosages used were high.

Carcinogenicity

A 20 percent solution of pentachlorophenol dissolved in benzene and applied dermally did not increase the rate of papillomas in mice pretreated with dimethylbenzanthracene (DMBA) (Boutwell and Bosch, 1959). The initiator (DMBA) was applied once and the pentachlorophenol twice weekly for 15 weeks. Seven percent of the controls and 4 percent of the PCP group developed papillomas. Neither group developed carcinomas. The exposure rate was 5 mg PCP per treatment applied in one drop to an unspecified skin area.

Mice dosed with commercial PCP at 46.4 mg/kg from 7 to 28 days of age and then fed 130 ppm PCP in the diet for the remainder of their life span (approximately 18 months) did not have a significant increase in tumors (Innes, et al. 1969). Detailed results were not published. The study used 18 male and female mice of each of two strains for a total of 72 mice.

Low nonphenolic content pentachlorophenol was non-carcinogenic when male and female Sprague-Dawley rats were fed 1, 3, 10 or 30 mg/kg for 22 months (males) or 24 months (females). The results are summarized in Table 7. Each sex dose group contained 25 animals (Schwetz, et al. 1978). The NOEL level based on clinical chemistry and hematology

determinations, routine histopathology and organ weight changes was 3 mg/kg in females and 10 mg/kg in males. The NOEL of 3 mg/kg was used to calculate the criterion shown later in this document.

TABLE 7

Incidence of Primary Tumors (Based on Histopathological Diagnosis) in Rats Fed Pentachlorophenol (PCP) for 22 Months (Males) and 24 Months (Females) (From Schwetz, et al. 1978).

	Males					Females				
Dose: mgPCP/kg/day	0	1	3	10	30	0	1	3	10	30
Number of rats examined:	27	26	27	27	27	27	27	27	27	27
Number of rats with tumors:	11	13	13	12	11	27	26	25	25	25
Number of tumors:	17	14	17	15	61	62	67	42	63	63
Number of tumors/rats with tumors:	1.6	1.1	1.3	1.4	2.3	2.6	1.7	1.7	2.5	2.5
Number of morphologic malignant tumors:	1	3	2	1	0	2	7	2	3	2

CRITERION FORMULATION

Existing Guidelines and Standards

The maximum air PCP concentration established by the American Industrial Hygiene Association (1970) is 0.5 mg PCP or 0.5 mg NaPCP/m^3 for an 8-hour exposure (TLV). The Code of Federal Regulations 21, part 121, paragraph 121:2556 allows up to 50 ppm PCP in treated wood intended for use in contact with food.

A tolerance for PCP in food has not been established.

A no-adverse-effect level in drinking water of 0.021 mg PCP/l is suggested by the National Research Council (1977). The recommendation is based on a NOEL of 3 mg/kg in the 90-day to 8-month rat studies. A safety or "uncertainty factor" of 1,000 and a water consumption of 2 L/day were used in arriving at the level. The longer duration study of Schwetz, et al. (1978), the negative results of Innes, et al. (1969) for carcinogenicity and the results of human epidemology studies were apparently not available or not considered in setting the uncertainty factor.

Current Levels of Exposure

Based on an assumed food consumption of 1.5 kg and a water intake of 2.0 kg, a food PCP residue of 10 ug/kg, and a water PCP residue of 60 ng/kg, the resulting maximum total daily exposure for a 70 kg person would likely be 15 ug from food and 120 ng from water. The exposure rate would be 0.21 µg/kg/day from food and 1.7 ng/kg/day from water. The food residue level estimated (15 µg) is higher

than the 1 to 6 µg/day intake calculated by Manske and Corneliussen (1974) where the calculations took into consideration dietary consumption by food class.

An alternative approach to estimating human exposure is extrapolation from urine residue data since PCP is primarily eliminated in the urine and at equilibrium excretion equals daily intake. In Hawaii, where exposure for general population may be higher than persons living in colder climates due to differences in use of PCP treated wood in home construction, Bevenue, et al. (1967a) reported an average PCP urine value of 40 µg/L. Assuming a daily urine void of 1.4 L the total daily PCP excretion would be 56 ug, an amount equal to the intake. Cranmer and Freal (1970) found an average of 5.8 µg/L in six general population urine samples and Kutz, et al. (1978) reported an average of 6.3 µg/L for 416 samples. Consequently, location of residence may influence PCP exposure. Based on available data, the exposure for the general population is estimated to range from 1 to 50 µg/person/day.

Exposure will increase sharply if an individual works with the material and inhales vapors and/or experiences dermal absorption (Casarett, et al. 1969; Bevenue, et al. 1967a). In the two subjects studied following a brush application, the urine PCP concentrations peaked at 300 to 500 µg/L.

Occupationally exposed individuals excrete more PCP in the urine than does the general population. Reported urine values include an average of 1.8 mg/L for 130 pest

control operators (Bevenue, et al. 1967b); 1-10 mg/L for wood treaters (Casarett, et al. 1969); 2.8 mg/L for dip treaters, 0.98 mg/L for spray treaters and 1.24 mg/L for pressure treaters (Arsenault, 1976). Using the same assumption of 1.4 L of urine per day the estimated occupational exposures would range from 1.37 to 14 mg/person/day.

Special Groups at Risks

Two groups can be expected to encounter the largest exposures. There are a small number of employees involved in the manufacture of PCP. All of these are presently under industrial health surveillance programs.

The second and larger group are the formulators and wood treaters. Exposure, hygiene and industrial health practices can be expected to vary from the small treaters to the larger companies. Health related data in general are not available for this group. Employees of two Hawaii wood treating companies have been studied for a number of years and although exposures have resulted in blood and urine levels of 1-10 mg/L, adverse health effects have been minimal.

Basis and Derivation of Criterion

Based on available and cited literature, PCP is not considered to be carcinogenic.

A criterion can be calculated using the data from the chronic toxicity studies. Using a NOEL of 3 mg/kg for low non-phenolic PCP and applying a 0.01 animal to human uncertainty factor the upper limit for non-occupational daily exposure is 0.03 mg/kg or 2.10 mg/70 kg person.

For the purposes of establishing a water quality criterion, human exposure to PCP is considered to be based on ingestion of 2 liters of water and 18.7 g of fish. The amount of water ingested is approximately 100 times greater than the amount of fish consumed. However, fish bioaccumulate PCP from water by a factor of 58 and thus contain about half as much PCP per gram as water.

With these considerations in mind, the following equation has been established:

$$2\ L \cdot X + (0.0187 \times 58) \cdot X = 2.10\ mg$$

Where:

2.10 mg = limit on daily exposure for a 70 kg person (ADI)

2 L = amount of drinking water consumed

0.0187 kg = amount of fish consumed

58 = bioaccumulation factor

Solving for X:

$$X = 0.68\ mg/l$$

Thus, 1.4 mg of the ADI can be obtained from 2L of drinking water and 0.7 mg from ingested fish.

Present food residues of PCP are reported to be 0 to 10 ug/kg and one report of 0.06 ug/kg in water. These levels are well below the criterion and total daily general population exposures are less than 1 percent of the calculated maximum value based on toxicologic considerations.

It should be noted that the criterion recommended in this document is based on a NOEL of low non-phenolic PCP, a compound found to be non-carcinogenic at the dosages tested. However, NCI is presently conducting studies on the carcinogenicity of PCP contaminants, hexachloro-p-dioxin, and octachloro-p-dioxin, the results of which are not yet available. The results of these studies should be evaluated before any EPA regulatory standards are established.

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